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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,702	11/25/2003	Elfatih Elzein	01-157-CIP	7434

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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,702	ELZEIN ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-33 is/are pending in the application.

4a) Of the above claim(s) 24-26 and 28-33 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-23 and 27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/16/2004.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 11/02/2005.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121:

I. Claims 1-23 and 27, drawn to an adenosine prodrug and its composition, classified in class 536, subclass various.

II. Claims 28-33, drawn to a process for the preparation of 2-adenosine C-pyrazole compounds, classified in class 536, subclass various.

III. Claims 24-26, drawn to a method of treating a disease with the compounds of Group I, classified in class 514, subclass various.

The inventions are distinct, each from the other because of the following reasons:

Groups I to II are related as product and process of making. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for making the product as claimed can be practiced with another materially different process or (2) the product as claimed can be made in a materially different process of making that product (MPEP § 806.05(h)). In the instant case the claims are drawn to the process of preparing 2-adenosine C-pyrazole compounds, indicating that the product can be prepared by a materially different process. See Klotz et al. (IDS dated 8/16/04):

the preparation of 2-adenosine C-substituted compounds is disclosed (page 104, material and page 105, Fig 1).

Groups I to III are related as product and process of using. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for making the product as claimed can be practiced with another materially different process or (2) the product as claimed can be made in a materially different process of making that product (MPEP § 806.05(h)). In the instant case the process for making the product can be practiced with another materially different product i.e. a method for using 2-adenosine C-pyrazole compounds as a potent agonists for A3 adenosine receptor can be practiced with another materially different product such as N6-adenosine substituted compounds (see Baraldi et al., Abstract, IDS dated 8/16/04).

Invention II to III, is unrelated to one another. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Group II is drawn to a process for the preparation of 2-adenosine C-pyrazole compounds, which is unrelated to method of treating a disease, of Group III.

Although the inventions are classified in the same class and sub-class, searching the three groups of inventions constitutes a burdensome search, as a thorough search comprises a search or foreign patents and non-patent literature as well as the

appropriate U.S. patent classifications. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their divergent subject matter, restriction for examination purposes as indicated is proper. It is noted that the four independent and distinct inventions would indeed impose an undue burden upon the examiner in charge of this application.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143). If applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims, which depend from or otherwise include all the limitations of the allowable product claim will be rejoined. (MPEP § 821.04).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so**

may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

A telephone call was made to Elin Hartrum on 10/31/2005 to request an oral election to the above restriction requirement. During telephone conversation with Elin Hartrum on 11/2/2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-23 and 27. Affirmation of this election must be made by applicant in replying to this Office action. Claims 24-26 and 28-33 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-23 and 27 are currently pending in this application.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6,11,13,15,16, 20-22 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the absence of the specific moieties intended to effectuate modification by substitution or attachment to the chemical core claimed, the term "substituted" in all occurrences renders the claims in which it appears indefinite wherein applicant fails to articulate by chemical name, structural formula or sufficiently distinct functional language, the particular moieties applicant regards as those which will facilitate substitution, requisite to identifying the compound of matter claimed.

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-23 and 27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Zablocki et al. (claims 1-28 of U.S. Patent No. 6,214,807; claim 1 of U.S. Patent 6,855,818; and claims 1,5 and 6 of U.S. Patent 6,770,634) in view of Klotz et al. (Naunyn-Schmiedeberg's Arch Pharm (1999), 360,103-108).

The instant invention is directed to a compound of the formula I (adenosine prodrug, claim 1) wherein C-2 is substituted pyazolyl or substituted triple bond (-C≡C-). Additional

limitations include and a pharmaceutical composition, in a pharmaceutically acceptable carrier, N-6 is substituted with an alkyl or aryl group, pyrazole group is substituted with a methoxyphenyl, a benzyl, a chlorobenzylaminocarbonyl or a pyrid-2-yl (specifically in claims 7-10,12,14,17 and 18) and triple bond (-C≡C-) is substituted with a phenyl and alkylene groups (specifically in claim 23).

Like the instantly claimed invention, the Zablocki et al's patents discloses the 2-adenosine C-pyrazole compounds and compositions wherein pyrazole is substituted with aryl and heteroaryl groups (see claim 1). The 2-adenosine C-pyrazole compounds are within the scope of the instant claims. The instantly claimed invention differs from the Zablocki et al's patents by claiming adenosine derivatives wherein C-2 is substituted with a substituted triple bond (-C≡C-). It is noted that Zablocki et al. do not disclose the N-substitution at C-6.

The Klotz et al. disclose 2-substituted N-ethylcarboxamidoadenosine derivatives (see abstract). Klotz et al. disclose a substituted triple bond (-C≡C-) substitution with alkyl chains and aryl groups at C-2 in adenosine (page 105, fig 1). Klotz et al also disclose the N-6- aryl substitution in adenosine derivatives (page103, 2nd col., last para.). Therefore the claims are co-extensive.

The examiner notes the instant claims and the Zablocki et al.'s patents claims do indeed substantially overlap and this obviousness-type double patenting rejection is necessary to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 1-23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zablocki et al. (U.S. Patent No. 6,214,807) in view of Klotz et al. (Naunyn-Schmiedeberg's Arch Pharm (1999),360,103-108).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The instant invention is directed to a compound of the formula I (adenosine prodrug, claim 1) wherein C-2 is substituted pyazolyl or substituted triple bond (-C≡C-).

Dependent claim limitations include and a pharmaceutical composition, in a

pharmaceutically acceptable carrier; N-6 is substituted with an alkyl or aryl group; pyrazole group is substituted with a methoxyphenyl, a benzyl, a chlorobenzylaminocarbonyl or a pyrid-2-yl (specifically in claims 7-10,12,14,17 and 18); and triple bond (-C≡C-) is substituted with a phenyl and alkylene groups (specifically in claim 23).

Like the instantly claimed invention, the Zablocki et al's patent teaches the 2-adenosine C-pyrazole compounds and compositions wherein pyrazole is substituted with aryl and heteroaryl groups (see claim 1). The 2-adenosine C-pyrazole compounds are within the scope of the instant claims. The instantly claimed invention differs from the Zablocki et al's patent by claiming adenosine derivatives wherein C-2 is substituted with a substituted triple bond (-C≡C-). It is noted that Zablocki et al. do not disclose the N-substitution at C-6.

The Klotz et al. disclose 2-substituted N-ethylcarboxamidoadenosine derivatives (see abstract). Klotz et al. disclose a substituted triple bond (-C≡C-) substitution with alkyl chains and aryl groups at C-2 in adenosine (page 105, fig 1). Klotz et al also disclose the N-6- aryl substitution in adenosine derivatives (page103, 2nd col., last para.).

It would have been obvious to person having ordinary skill in the art at the time the invention was made having the above-cited references before him, to select pyrazole for variable R^2 in 2-adenosine compounds as taught by Zablocki et al. or a triple bond (-C≡C-) for variable R^2 in 2-adenosine compounds as taught by Klotz et al., because Zablocki et al. disclosed that A_3 receptors are involved in a mast cell degranulation and,

therefore, asthmatics are not given the non-specific adenosine to induce a pharmacological stress test (col. 1, lines 31-33).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is 571-272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 571-272-0661. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD.
Art Unit 1623
August 8,2005

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600